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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,595	06/07/2002	Albrecht E. Sippel	WEICKM 14	5887

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EXAMINER

GAMETT, DANIEL C

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,595	SIPPEL ET AL.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 8, 10-13, 15-20, 22-71 and 74-82 is/are pending in the application.
- 4a) Of the above claim(s) 11-13, 29, 38, 44-60, 64-66, 71 and 74-78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 8, 10, 15-20, 22-28, 30-37, 39-43, 61-63, 67-70 and 79-82 is/are rejected.
- 7) ☒ Claim(s) 81 is/are objected to.
- 8) ☒ Claim(s) 1-4, 8, 10-13, 15-20, 22-71 and 74-82 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/17/2005 has been entered.
2. Claims 11-13, 29, 38, 44-60, 64-66, 71, and 74-78, are withdrawn from consideration as being drawn to a non-elected invention. Claims 5-7, 9, 14, 21, 72, and 73 are cancelled. New claims 81 and 82 have been added. Claims 1-4, 8, 10, 15-20, 22-28, 30-37, 39-43, 61-63, 67-70, and 79-82 are under examination.
3. All prior objections/rejections not specifically maintained in this office action are hereby withdrawn.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Claim Objections

5. Claim 81 objected to because of the following informalities: It appears that Applicant intends the claim to read "...and subjecting it *to* the method..."; the word *to* is omitted. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. Rejection of claims 1-4, 8, 10, 15-20, 22-28, 30-37, 39-43, 61-63, 67-70, 79, and 80 as failing to comply with the written description requirement, set forth in the office action mailed 06/17/2005, is maintained and hereby extended to include claims 81 and 82. Applicant's arguments filed 09/19/2005 have been fully considered but they found to be persuasive only in part. Applicant argues that in view of *Capon v. Eschhar* it is not necessary to include sequences that were well known in the art at the time of filing. It is conceded that the art provides the information necessary to construct many fusion proteins with membrane localization signals, steroid receptor hormone binding domains, and Ras proteins. Applicant's claims, however, are drawn to a genus of fusion proteins that are not described in the prior art or in the instant specification. Any sequence that retains as little as two consecutive amino acids from the reference sequence could meet the limitation "*an* amino acid sequence" in claims 1 and 82. Even if claim 1 were amended to recite "*the* amino acid sequence", claim 8 would still permit unlimited variability of the structure of the second domain. This greatly expends the genus of claimed fusion proteins and exacerbates the inadequacy of the single example to provide sufficient distinguishing identifying characteristics of the genus.

7. Rejection of claims 1-4, 8, 10, 15-20, 22-28, 30-37, 39-43, 61-63, 67-70, 79, and 80, under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, set forth in the office action mailed 06/17/2005, is maintained and extended to include claims 81 and 82, with modifications as follows.

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8. The specification, while being enabling for a fusion protein consisting of a myristylation signal, amino acids 282-595 of the human estrogen receptor, and human ha-ras (L61) without a CAAX box, does not reasonably provide enablement for fusion proteins comprising any other amino acid sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The unpredictability of the art of constructing fusion proteins with activities that are regulated by steroid hormone binding domains was established in the office action mailed 12/17/2004. While the scope of the claims has narrowed, it remains true that each embodiment of the claimed fusion protein needs to be characterized individually and that one working example is not enabling for the scope of the claims. The genus of potential occupants of all three domains of the fusion proteins is greatly expanded by the indefinite article *an* in claims 1 and 82, for example. This open language encompasses an impermissibly large number of sequences, some of which could comprise as little as two consecutive amino acids from a naturally occurring protein, each of which would have to be tested for the functional capability recited for each domain. This could be obviated by use of the definite article *the*, which would specify sequences recognized to have the recited function. As currently claimed, the second domain may be derived from receptors for any of estrogen, progesterone, androgens, glucocorticoids, mineralocorticoids, or Vitamin D3. Claim 8 recites no limitations on the extent to which a reference sequence may be mutated, and therefore it broadens the scope of the claim far beyond the enabled scope. Claim 43 still recites “nuclear receptor” and so the enablement issues that stem from the breadth of this term, of record, apply to this claim. Finally, claim 63

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still recites the alternative “when there is binding of a ligand to the second domain” the third domain cannot exert activity, which is not enabled for reasons of record.

9. Claims 8, 10, and 81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 8 recites the fusion protein of claim 1 but then provides a definition for the second domain that is inconsistent with that of claim 1. The question of when an amino acid sequence that is derived from the sequence of a naturally occurring steroid receptor (claim 8) ceases to be an amino acid sequence of the receptor (claim 1) is debatable, and therefore the claim is indefinite. If, as suggested, claim 1 were amended to recite *the* amino acid sequence of..., any derived sequence recited in claim 8 would lack antecedent basis. It is suggested that, if Applicant wishes to claim mutated or derived sequences, claim 1 should be amended to provide for variants, or claim 8 should be amended or rewritten as an independent claim. Applicant should further note that this question of clarity is separate from the questions of written description and enablement that arise with any claim to variant sequences.

11. Claim 10 is drawn to a fusion protein of claim 1 in which the third domain has the activity of a constitutively active Ras protein. This suggests that the third domain is constitutively active, which is contradictory to claim 1 which seems to describe the third domain as being regulated by ligand binding to the second domain.

12. Claim 81 is drawn to the method of claim 36, further comprising derivatizing said test substance identified in said method. Claim 36 is a method to identify ligands; the correlation step

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of the method of claim 36 states that “detection of the activation of the signal pathway connected to a Ras protein indicates the ability of the test substance to bind to the second domain of the fusion protein”. Therefore, the test substance of claim 81 is, by definition, a ligand, as reiterated in claim 81a). It is not clear what additional or alternative properties of the test compound are intended by b) and c) of claim 81. Limitation b) recites “a compound able to alter the ability of a ligand-binding section of said steroid receptor”. It is not clear what ability is being referred to here. Limitation c) recites “ a polypeptide having ligand-binding activity for said steroid receptor”. This might mean that the ligand is a polypeptide. The wording of claim 81c), however, seems to indicate a polypeptide with the same ligand binding activity as the steroid receptor. It is conceivable that such a polypeptide could influence the outcome of the assay recited in claim 36, but its logical effect would be the opposite of a ligand, because it would competitively prevent any actual ligands from binding to the fusion protein. Thus, such a polypeptide would not be identified in the method of claim 36. By this interpretation, limitation c) has no antecedent basis within claim 81 or in claim 36.

Conclusion

13. No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG

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3 February 2006

David S. Romeo
DAVID S. ROMEO
PRIMARY EXAMINER